LIVERPOOL SCHOOL OF TROPICAL MEDICINE

SCIENTIFIC RECORD

COMPILED BY

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PLATES I—IX

The new laboratories of the Liverpool School of Tropical Medicine were formally opened on 24th July, 1920, by Lord Leverhulme, Honorary Vice-President and former Chairman of the School.

The building had been placed, in 1915, at the disposal of the Military authorities for the purposes of a hospital, and was used by them until 1919, for the treatment of patients suffering from tropical diseases, mainly malaria and dysentery. The hospital, which consisted of about 200 beds, was under the charge of Lieut.-Col. J. W. W. Stephens, R.A.M.C., Professor of Tropical Medicine, and during its four years' existence more than 3,000 cases were admitted.

Subsequent to evacuation by the Military authorities, the decoration and equipment of the laboratories were put in hand, and to-day the School affords excellent conditions and facilities for instruction and research.

The laboratories are situated in the University grounds, and close to the Royal Infirmary, in which the School has its Tropical Ward and adjoining clinical laboratory. In addition to the basement, which contains the Photographic Department and large storage rooms, there are four floors. The ground floor comprises the Lecture Theatre, with accommodation for about seventy students; the Library, where, besides text-books and miscellaneous scientific publications, over one hundred current medical journals from all parts of the world can be consulted; and the Museum, a spacious room, 80 feet by 69 feet, with preparation room adjoining.

On the first floor are the Departments of Tropical Medicine and Entomology, the latter with its library of specialised literature, and six research rooms. The second floor comprises the excellently lighted class laboratory, 69 feet by 58 feet, and four research rooms devoted to the Department of Parasitology, while the third floor has a large research laboratory and two smaller research rooms. On the roof are an Insectarium, a mosquito-proofed house, and the animal houses.

The occasion of the official opening was marked by the issue of a volume* which traces the history of the School from its foundation down to the year 1920. The main purpose of this publication was to perpetuate the names of those who have been closely associated with the School in its varying activities in the past, and this aspect may here be briefly summarised before proceeding to an account of its scientific activities which, in the 'Historical Record,' are merely outlined.

The Liverpool School of Tropical Medicine was founded in 1898 by the late Sir Alfred Lewis Jones, K.C.M.G., a prominent Liverpool ship-owner, who, fired by an appeal for the study of tropical diseases issued by the late Rt. Hon. Joseph Chamberlain, then Secretary of State for the Colonies, offered to the President of the Royal Southern Hospital the sum of £350 for three years, to promote the special study of such diseases. Quarters were obtained in the Pathological Department at the University, and a Dean was appointed in the person of Professor Rubert Boyce, to whose tireless energy much of the early success of the School was due. In February, 1899, Dr. H. E. Annett was appointed Demonstrator in Tropical Pathology; in April, Major Ronald Ross accepted the post of Lecturer, and the School was officially opened; and in May teaching commenced.

The early history of the Liverpool School is a record of struggle; it was not founded by the Government, as was the London School; it had no grant, no assured income, nor even, at first, Government recognition. The School early turned its attention to research, and in the summer of 1899 the first of its expeditions was despatched to Sierra Leone. During the next fourteen years funds were

* Liverpool School of Tropical Medicine: Historical Record, 1898-1920. *At the University Press*, 1920. viii, 103 pp., 36 plates. 10/6 post free.

collected to equip and maintain more than thirty expeditions to various tropical regions, including West and Central Africa, Brazil and the West Indies.

In the meanwhile, at home the School was enlarging its scope and consolidating its position. In 1900 the Government gave it full recognition by placing it on the same terms as the London School with regard to newly-appointed medical officers and their courses of training, and four years later further recognition was received in the form of a financial grant from the Colonial Office, which grant was later increased and has continued to the present day. In 1901 a Lectureship and Fellowship were founded, in commemoration of the work of the late Walter Myers, who died of yellow fever in Brazil while serving with the Fourth Expedition. Major Ross was appointed to the former, and the latter was filled by Dr. J. E. Dutton, who, four years later, died in the Congo while investigating tick fever. In 1903 the Alfred Jones Chair of Tropical Medicine was founded, the first holder being Major Ross, while Dr. J. W. W. Stephens, who had joined the staff in the previous year, was appointed to the vacant Walter Myers Lectureship. In 1905 another important Lectureship was founded, namely, that of Economic Entomology, which was accepted by Mr. R. Newstead, of Chester. As the work and influence of the School increased, many new appointments were made, so that now, at the age of twenty-two, the School has three University Chairs,* namely, Tropical Medicine, Entomology and Parasitology, filled by Professors Stephens, Newstead and Yorke, respectively, assisted by a staff of eight Lecturers.

In 1903 the School moved into new laboratories, and in the following year a Diploma in Tropical Medicine was instituted.

In 1904 the Runcorn Research Laboratories were established for the purpose of conducting investigations on the large collection of trypanosomes and other protozoa, which had been amassed by members of the expeditions on various occasions. These laboratories were first placed in the charge of Dr. Wolferstan Thomas, and during their ten years' existence much valuable research was done there.

* A fourth Chair, that of Tropical Diseases of Africa, has now (1921) been established, and is held by Professor B. Blacklock.

In 1906 was issued the first number of the *Annals of Tropical Medicine and Parasitology*. This publication had been preceded by a series of twenty-one *Memoirs*, mostly reports of the School's expeditions.

In 1911 the Yellow Fever Bureau came into being with Dr. Harald Seidelin as Director. As the name implies, the Bureau was established for the purpose of promoting the study of the many problems surrounding this disease. A journal was issued, the *Yellow Fever Bulletin*, of which three volumes were published.

Clinical instruction to students of the School had formerly been given in a special ward at the Royal Southern Hospital. This hospital being at some distance from the laboratory, arrangements were subsequently made with the Royal Infirmary for the erection of a new tropical ward in the Infirmary grounds. The ward, which contains ten beds, with an adjoining clinical laboratory, was opened in 1914.

On the arrival of the Fifteenth (Yellow Fever) Expedition at Manáos in 1905, it was found necessary for the work of the Expedition to establish a laboratory of a more or less permanent character. The Manáos Research Laboratory remained in existence until January, 1909, when, owing to the return of its Director, Dr. Wolferstan Thomas, to Liverpool, it was closed. In June, 1910, Dr. Thomas returned to Manáos and opened the present laboratory. In 1914 it was decided to extend the activities of this branch of the School; the outbreak of war, however, caused all developments to be deferred until 1919, when three research assistants were appointed to the laboratory.

With a view to carrying on research work in tropical medicine, the School desired to establish a permanent laboratory on the West Coast of Africa. Funds were available, through the munificence of the late Sir Alfred Jones, and a suitable site on Tower Hill, Freetown, Sierra Leone, having been placed at the disposal of the School by the Colonial and War Offices, the laboratory is now in course of erection.

FIRST LABORATORY OF THE SCHOOL

The following brief record of the research work of the School is dealt with under subjects; no attempt at a critical estimate has been made.

MALARIA AND SANITATION

The first Expedition left England in July, 1899, for Sierra Leone, and consisted of Major Ross, Dr. H. E. Annett, Dr. R. Fielding-Ould, Mr. E. E. Austen, officially appointed by the British Museum, and Dr. Van Neck, delegate of the Belgian Government to the School. The purpose of the Expedition was to study malaria in man, and a report of the work accomplished was published in 1902 as *Memoir* II. The investigators discovered two species of *Anopheles* in Freetown, namely, *A. funestus*, Giles, and *A. costalis*, Loew, and by dissection established the presence of blasts (sporozoites) in them. They concluded that both *A. costalis* and *A. funestus* are hospitable to the human Haemamoebidae; that *A. costalis* is hospitable to all three of the human species, and *A. funestus* certainly to *H. malariae*, and probably *H. vivax*; no observations were made regarding the connection of *A. funestus* with *H. praecox*. They further pointed out the difference between *Culex* and *Anopheles*, and studied more especially the bionomics of the latter. 'Precautions against the bites of gnats' and 'operations for reducing the number of *Anopheles*' were fully considered. Dr. Fielding-Ould continued the work of the Expedition at Freetown after the other members had returned to England, and he also prosecuted his researches at Accra and Lagos, his report of which is included in *Memoir* II. At Freetown six of twenty-nine *Anopheles* dissected showed parasites. Seventeen *Culex* gave negative results. At Accra fifty-two *Culex* were negative. At Lagos thirty-seven *Anopheles* were dissected and zygotes found in one. The reports dealt mostly with the sanitary survey of the districts.

In 1900 a third Malaria Expedition was sent to Northern and Southern Nigeria. This Expedition, which was composed of Drs. H. E. Annett, J. E. Dutton and J. H. Elliott, spent six months in Nigeria, and in *Memoirs* III and IV reports were published of the work done, the former relating to malaria and the latter to filariasis (see p. 37). Seven of two hundred and eighty-one *Anopheles*

dissected at Bonny were found to be infected with malaria; it was noted that it was difficult to decide what was the exact type of parasite present. The observation made by Koch and by the Royal Society's Commission that native children are infected with malarial parasites to a large degree was confirmed; the incidence of infection is given in the following table. It was also proved that

TABLE showing the total number of children examined and found infected throughout Nigeria.

Ages	Number examined	Number infected	Percentage infected
0-5	220	114	51·8
5-10	108	27	25·0
10+	40	4	10·0

quartan and simple tertian parasites exist in West Africa, a fact contrary to the experience of the Royal Society's Commission of the previous year. The bionomics of *Anopheles* were studied still further and a series of experiments in propagation carried out, confirming and elaborating the discovery of the previous Expedition that the female mosquito requires a meal of blood both for fertilisation and for the development of the ova. In their recommendations concerning prophylaxis they advocated (1) the segregation of Europeans at a distance of about half a mile (a principle already put forward by the Royal Society's Commission on Malaria also at work in West Africa), and (2) the surface drainage of areas around their quarters. In an appendix they gave charts and descriptions of cases of hyperpyrexial fever, first described by Thompstone and Bennett. The hyperpyrexial stage lasts one to three weeks, and is followed by very extended lysis. An exhaustive account was given in the second report (*Memoir* IV) of the mouth parts of the female *A. costalis*, and, in an appendix by Theobald twenty-five mosquitoes were described of which nine were new species, namely, *Stegomyia irritans*, *S. nigricephala*, *Culex duttoni*, *C. decens*, *C. pruina*, *C. invenustus*, *C. nebulosus*, *C. rima* and *C. invidiosus* (with figures).

In June, 1901, Major Ross and Dr. Logan Taylor went to Freetown to organise an anti-mosquito campaign. Work was

commenced by engaging the services of between thirty and forty men, who were divided into two gangs: the *Culex* gang and the *Anopheles* gang. The former collected from private houses all the broken bottles and buckets, empty tins, etc., in which *Stegomyia* and *Culex* breed; the latter drained the pools and puddles in which *Anopheles* breed in the streets and backyards of the houses. Reports on the progress of this campaign were published as *Memoir* V, Parts 1 and 2, and later Ross issued a small book: 'Mosquito Brigades, and how to organise them.'

In September, 1901, Dr. Dutton went to the Gambia and inspected the conditions of health there, with the result that the Colony organised measures similar to those in operation at Freetown (*Memoir* X). About 32 per cent. of the infections examined

TABLE showing the total number of children examined and found infected throughout the Gambia.

Ages	Number examined	Number infected	Percentage infected
0-5	78	64	82·0
5-10	22	20	91·0
10+	13	7	53·8

showed quartan parasites, and about a third of the malignant tertian cases showed crescents. The simple tertian parasite was found three times only.

Dutton noted the universal infection of canaries with *Halteridium*, which was also found in other birds.

Of twenty-four *A. funestus* dissected, one contained sporozoites and one zygotes.

A. costalis was found breeding in boats, street drains, wells, tubs and barrels, and in tidal water containing 1·7 per cent. salt, together with *C. thalassius*. It would appear that *A. funestus* and its varieties are rural mosquitoes, while *A. costalis* is essentially town bred and capable of utilising any small collection of water for breeding purposes.

In an appendix, descriptions of eighteen species were given by Theobald, including *A. costalis*, var. *melas*; *A. funestus*, var.

umbrosus; *A. funestus*, var. *subumbrosus*; *Stegomyia albocephala*, sp. n.; *Culex annulioris*, var. *gambiensis*, v. n.; *C. anarmostus*, sp. n.; *C. thalassius*, sp. n.; *C. euclastus*, sp. n.; *Lasioconops poicilipes*, gen. n., sp. n.; *Corethra ceratopogones*, sp. n. Eight specimens of *G. longipalpis* var. *tachinoides* were taken. Dutton recorded the finding of a filarial embryo in the thoracic muscle of *C. anarmostus*.

It was during his researches into the blood parasites of the Gambia that Dr. Dutton made a discovery of the highest scientific importance, namely, the identification for the first time of a trypanosome in the blood of a man, a patient of Dr. Forde. This parasite was subsequently (see p. 16) shown to be the cause of sleeping sickness, and was named ***Trypanosoma gambiense***, Dutton, 1902.

In 1901, Dr. C. Balfour Stewart was sent to the Gold Coast, to conduct operations similar to those carried on at Sierra Leone, while early in 1902 Major Ross again visited Freetown to ascertain by a thorough inspection the results of the previous Expedition. In the autumn of this year, Dr. Logan Taylor proceeded to Cape Coast Castle, Gold Coast, and reported upon the sanitary conditions prevailing there, with suggestions as to their improvement. (*Memoir* VIII).

In September, 1902, by request of the Suez Canal Company, Major Ross went to Ismailia to investigate the causes of the prevalence there of malaria, and to recommend measures for its prevention. *Anopheles* and *Culex* were found breeding in water containing 0·9 per cent. of salt. He concluded that the majority of *Anopheles* which caused malaria in Ismailia came from the marshes in immediate proximity to the town. Prophylactic measures based on his recommendations were commenced immediately (*Memoir* IX). In February, 1904, sixteen months later, Professor Boyce visited Ismailia; from statistics furnished in his report (*Memoir* XII), it appeared that the number of cases of malaria had fallen from 1,551 in 1902, to 209 in 1903.

During 1904, two Sanitary Expeditions were despatched to West Africa: one to Bathurst, Conakry and Freetown, and the other to the Gold Coast. Reports were published in 1905 as *Memoirs* XIV and XV.

In May, 1906, Professor Ross went to Greece in order to advise

SECOND LABORATORY OF THE SCHOOL

the Lake Copais Co. with regard to anti-malaria measures. In the following year, at the request of the Colonial Office, he visited Mauritius for the same purpose; his report, entitled 'The Prevention of Malaria in Mauritius,' was published in 1908 (Waterlow & Sons).

In 1908, the Twenty-first Expedition of the School, consisting of Professor Newstead, Dr. W. T. Prout and Dr. Alan Hanley, was despatched to Jamaica. Reports were published in the *Annals of Tropical Medicine and Parasitology*, Vol. III, pp. 421 and 471, the first, dealing with medical and economic entomology, by Professor Newstead (see p. 39), the second, on malaria, by Dr. Prout. From data furnished by Dr. Neish, of Spanish Town, the frequency of the various species of malaria parasite was found to be approximately: simple tertian 54 per cent., malignant tertian 36 per cent., quartan about 1 per cent., and mixed infections about 8 per cent. The occurrence of several cases of blackwater fever was noted. The enlarged spleen rate in different parishes varied from 0 to 60 per cent. Prout found that the average percentage of malarial deaths to total deaths was nearly 20 per cent., that in four years the total admissions to hospitals from malaria had increased by 55 per cent., and that over 33 per cent. of the total admissions were due to malaria; it was reported that the annual cost of treating malarial patients was over £6,000. Various anti-malarial measures were recommended. In 1909, Boyce visited Jamaica, and reported upon the work done by the Commission appointed by the Governor in October, 1909, to deal with the malaria problem (*Annals*, Vol. IV, p. 233). It was recorded that one-half of the island, namely, those parts above 1,000 feet, was practically free from malaria-carrying mosquitoes.

Ross and D. Thomson, working in Liverpool, published a paper entitled 'Some Enumerative Studies on Malarial Fever' (*Proc. Roy. Soc.*, B., Vol. LXXXIII, p. 159, and *Annals*, Vol. IV, p. 267). Some of the conclusions were: (1) No fever exists unless the parasites exceed from 500 to 1,500 per c.mm.; (2) the parasites tend to remain continuously in the blood in small numbers between the febrile relapses; (3) close correlation between the number of parasites and the amount of fever caused by them; (4) studies on quinine gave a numerical estimate of its effect, a few days' use of the drug reducing the parasites by from 50 per cent. to 80 per cent.;

(5) crescents apparently require eight to ten days for development; quinine affects their numbers only by destroying the generating cells. Thomson, who subsequently investigated the life history of crescents (*Annals*, Vol. V, p. 57), concluded that these do not live for more than a few days in the peripheral blood. They are replenished from surviving asexual forms, and quinine has no action on crescents but only on the asexual source of supply. He concluded (*Annals*, Vol. VI. p. 223) that administration of quinine in doses of 20 grains daily for three weeks is almost certain to destroy both the asexual and sexual parasites. In a study of the leucocytes in malarial fever (*ibid.*, p. 83), he stated that malaria could be diagnosed by the leucocytic formula.

In 1912, J. G. Thomson and McLellan confirmed Bass's observations on the cultivation of malarial parasites. In twenty-four hours *P. falciparum* was found to undergo segmentation, the maximum number of merozoites counted being thirty (*Annals*, Vol. VI, p. 449). In the case of *P. vivax* (*Annals*, Vol. VII, p. 153), sixteen merozoites were produced. These cultures of *P. vivax* differed from those of *P. falciparum* in that there was no tendency to clumping. Further experiments in the cultivation of *P. falciparum* and *P. vivax* were made (*ibid.*, p. 509), when it was noted that the optimum temperature for cultures was 38° C.

Sinton, investigating Uriola's test of malarial pigment in the urine (*Annals*, Vol. VI, p. 376), concluded that it is almost impossible to exclude extraneous pigment.

In 1912, Dr. David Thomson was sent to Panama to study certain malarial problems with Dr. James, Chief Assistant Physician to the Ancon Hospital. The first part of his report (*Annals*, Vol. VII, p. 125) dealt with the sanitation in the Canal Zone, Trinidad and British Guiana; the second (*Annals*, Vol. VIII, p. 85) with the origin and development of gametes in malignant tertian malaria. He noted that they develop chiefly in the bone marrow and in the spleen, the period of incubation being about ten days.

While examining a malarial blood film sent from the Central Provinces of India, Stephens was struck by the peculiar appearance of the parasite (*Proc. Roy. Soc.*, B. Vol. LXXXVII, p. 375, and *Annals*, Vol. VIII, p. 119). It exhibited the following peculiarities:

(1) it was extremely amoeboid; (2) the cytoplasm was scanty; (3) the nuclear protoplasm was out of proportion to the volume of the parasite. It differed from *P. falciparum* by its amoeboid activity, and from *P. vivax* by its smaller size, the delicate nature of its amoeboid processes, the irregularity of its chromatin and the rarity of typical ring forms. Stephens proposed to name this parasite *P. tenue*. Later he described peculiar forms of a malaria parasite in a blood slide from the Gold Coast (*Annals*, Vol. IX, p. 169). In addition to these, large and apparently quite normal quartan parasites occurred, and it was possible to trace a transmission from normal ring forms to those in which chromatin particles or strands without any protoplasm were seen in the red cells.

In 1917, the School was asked by the War Office to undertake investigations into the treatment of malaria; the results of this work were published in thirty papers (*Annals*, Vols. XI-XIII).

No case was considered to be malaria unless parasites were found. The results of treatment were in all cases controlled by daily microscopical examinations combined with the clinical record.

Simple Tertian. The investigators established: (1) that intramuscular injection of quinine bihydrochloride was an effective method of treating a malarial attack, a matter which had been one of considerable dispute in the medical press just previous to this work. (2) That for the palliative treatment of malaria, that is, for keeping a person free from relapses over long periods, it was better to give a certain total amount of quinine on each of two consecutive days than on each of six days in the week: thus, 60 grains administered as 30 grains for two days gives a better result than the same amount administered as 10 grains for six days. (3) The best palliative result was obtained by administration of 45 grains on each of two consecutive days weekly over a period of two months. (4) They found that a certain treatment may give a certain 'curative'* result on one occasion, while the same treatment repeated on another occasion might give a quite different result. (5) Novarsenobillon was found to be as efficacious as quinine in the treatment of paroxysms, but its curative effect, like that of quinine, was practically nil. (6) The best 'curative' result was obtained by

* The term cure was used to signify no relapse within an observation period of 60 days after cessation of treatment.

the administration of *Liquor arsenicalis*, minims 30, daily over a period of eight weeks in combination with two initial intramuscular injections of quinine bihydrochloride, grains 15, on two days only. Owing to the Armistice, these observations were not repeated.

The intravenous injection of quinine was found to have no real curative effect.

The relapse period after treatment of eight hundred simple tertian cases was recorded (*Annals*, Vol. XIII, p. 125). It is essential to recognise that these figures were based on an observation period of sixty days. The incidence is shown in the accompanying graphs. It will be seen that of those cases that relapse the majority do so in the first twenty days after cessation of treatment. Further, the time of occurrence of the paroxysms was noted in one thousand cases (*Annals*, Vol. XIV, p. 365). The majority occurred at 2 p.m. with the conditions of life under which the patients (soldiers) were living; over 90 per cent. occurred during the hours of activity, that is, between the hours of 7 a.m. and 6.59 p.m.

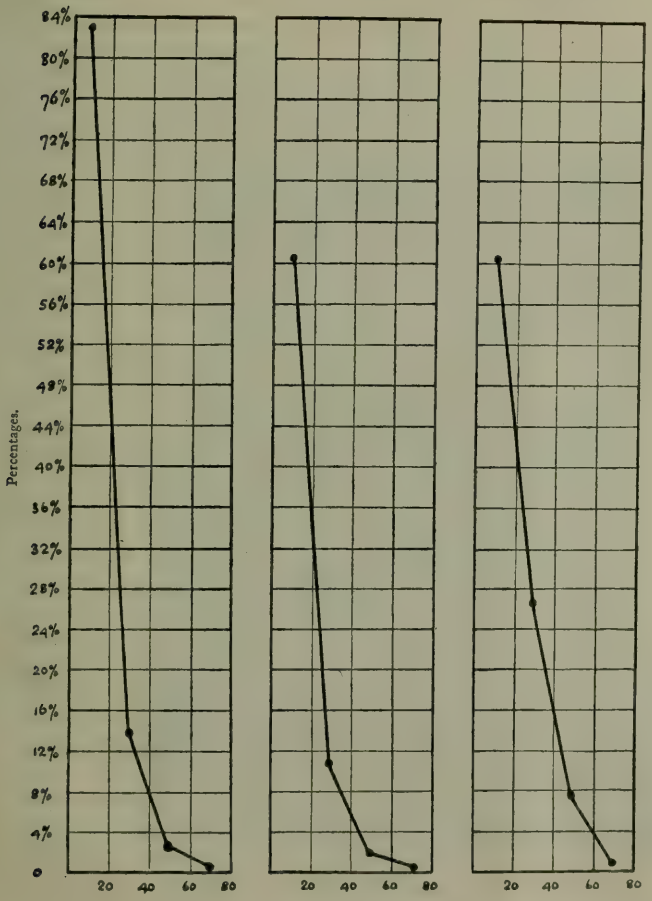
Malignant Tertian. Neither a single nor a series of six intravenous injections of quinine bihydrochloride (grains 10 to 15) caused the disappearance of parasites, either trophozoites or gametes, from the peripheral blood, whereas in the case of simple tertian the disappearance was rapid. Under quinine treatment, grains 30 to 45 daily, crescents did not persist in the peripheral blood in the majority of cases for more than three weeks. How long they persist without quinine was not determined.

In July, 1919, Blacklock and Carter recorded the experimental infection, for the first time, of *Anopheles plumbeus* with *P. vivax*. Experiments were made (*Annals*, Vol. XIII, pp. 187 and 413), with the result that the observers were able to obtain infections of the gut and salivary glands of laboratory-bred *A. plumbeus* at a temperature of 28° C.; at room temperature gut infection only was obtained. Infection of the gut was also produced with *P. vivax* in the case of *A. bifurcatus* at 28° C. Later experiments (*Annals*, Vol. XIV, p. 275) with *A. plumbeus* resulted in gut infection with oocysts of *P. falciparum* at 28° C.

GRAPH 1.
Percentage of total relapses in each 20-day period.

GRAPH 2.
Percentage of cases treated which relapse in each 20-day period.

GRAPH 3.
Percentage of cases treated not having previously relapsed which do so in each 20-day period.



BLACKWATER FEVER

In 1907, the Nineteenth Expedition, consisting of Dr. J. O. Wakelin Barratt and Dr. Warrington Yorke, was despatched to Nyasaland to study blackwater fever, a report being subsequently published in *Annals*, Vol. III, p. 1. The object of the investigators was to trace out some of the internal processes, the terminal event of which is the appearance of blackwater, believing that in that way many obscure points in connection with the causation and treatment of the condition would be cleared up. The first point was to determine the action of quinine, acid and alkali upon the red cells during blackwater fever. They found that haemolysins, present in the blood, played no part in the production of blackwater. It was considered that the suppression of urine is due to a mechanical blocking of the renal tubes by the formation of large, firm, coarsely granular casts in the ducts of Bellini. In a later study (*Annals*, Vol. V, p. 287), on the suppression of urine in blackwater fever, Yorke and Nauss re-investigated the mechanical theory and found that it is considerably facilitated by any factor which tends to lower the blood-pressure, and by that means the secretion of water by the glomeruli, but that if the blood-pressure is kept up by the injection of saline solutions, the tendency to suppression is decreased. Arising out of these latter experiments, the passage of haemoglobin through the kidneys was studied by Yorke (*ibid.*, p. 401), who was led to consider that haemoglobin is excreted by the renal epithelium rather than filtered through the glomeruli, and that the amount of haemoglobin eliminated into the urine is dependent upon the activity of the epithelium lining the renal tubules.

It was shown by Simpson (*Annals*, Vol. VI, p. 313) that the haemoglobin liberated from the red cells in malaria escapes in larger quantities by the faeces than by the urine. The study of haemoglobin metabolism in blackwater fever was continued, and a report made (*Bio-Chemical Journal*, Vol. V, p. 378) on the quantitative estimation of urobilin in the excreta. In later observations on haemolysis in malaria (*Annals*, Vol. VI, p. 231), Simpson concluded that the serum of malarial patients may possess the power of haemolysing normal red blood cells. The haemolytic effect could

FRONTAGE OF THIRD LABORATORY OF SCHOOL.

not be obtained at all periods of the paroxysm, nor in every case; it appeared to be produced at the period of sporulation, and rapidly disappeared. Simpson and Edie (*ibid.*, p. 443), observing the excretion of urobilin in animals and man, found that an increase may occur after the administration of quinine in doses of 10 to 30 grains a day, and that a similar result follows injection of blood pigment or haemolytic drugs.

Experiments were devised by Barratt and Yorke (*Annals*, Vol. VIII, p. 509) for examining the relation of bile pigments to haemoglobin. Experimenting with rabbits, they found that consequent upon intravenous injection of haemoglobin solution there was a distinct and immediate increase not only in the concentration of the bile pigment, but also in the amount of bile pigment excreted. Two hypotheses were advanced to explain this increase: (1) that the haemoglobin injected is actually converted by the liver into bile pigment; or (2) that it merely stimulates the liver cells to an increased production of bile pigment.

Stephens (*Thompson-Yates Lab. Reports*, Vol. V, Pt. 1, p. 193) recorded that blackwater fever occurred in eleven of twenty-two of the United States. An account was given of the distribution of the disease, and an extensive bibliography appended. An analysis of ninety-five cases showed that when the blood was examined before the onset of blackwater, malarial parasites were present in 95·6 per cent. of cases, whereas on the following day the remarkable fall to 17·1 per cent. was the result. On the day of blackwater itself the figure was 61·9 per cent.

A series of studies in blackwater fever were made by Stephens (*Annals*, Vol. VII, p. 479). The subject was considered under the following headings: (1) malarial parasites; (2) pigmented leucocytes; (3) post-mortem examinations; (4) influence of malaria; (5) relationship to species of malaria parasites; (6) effect of period of residence; (7) seasonal prevalence; (8) correlation between malaria and blackwater statistics; (9) second attacks. A schedule for recording cases of blackwater was devised and recommended (*Annals*, Vol. VIII, p. 639). The results were recorded (*Annals*, Vol. IX, p. 201) of a statistical examination of the respective times at which quinine was given and blackwater occurred. Graphs were published showing that correlation existed between the time of

taking quinine and the onset of symptoms, but this did not necessarily imply any relationship of cause and effect. Data on the duration of haemoglobinuria were collected (*Annals*, Vol. IX, p. 539). In one hundred and sixty-seven records it was found that the duration was not more than twelve hours in a quarter of the cases, not more than one day in half the cases, and not more than two days in three-quarters of the cases. Finally, the importance of furnishing population statistics in connexion with cases of black-water fever was emphasised (*Annals*, Vol. X, p. 345).

PIROPLASMOSIS

At Runcorn, Breinl and Hindle studied the morphology of *Piroplasma canis* (*Annals*, Vol. II, p. 233), and worked out the nuclear details of the parasite. Later, Breinl and Annett (*ibid.*, p. 383) concluded that the haemolysis in *Piroplasma canis* is not due to a formation of a specific haemolysisin or isolysin, but to the mechanical disintegration of the red blood corpuscles after the escape of the parasites from them. Barratt and Yorke found that in piroplasmosis the haemoglobinuria was attended with and dependent upon haemoglobinaemia. Of one hundred and forty-three cattle examined at Sierra Leone (*Annals*, Vol. IX, p. 418) about 5 per cent. were found to be infected with *P. bigeminum*, while *Theileria mutans* was encountered in between 20 and 30 per cent.

TRYPANOSOMIASIS

In view of the great importance of the discovery of the trypanosome in man by Dr. Dutton* in 1901, described and named by him *T. gambiense* (*Thompson-Yates Reports*, Vol. IV, p. 455), an Expedition was sent out to the Gambia and French Senegal in September, 1902, in charge of Dr. Dutton and Dr. J. L. Todd, for the study of Trypanosomiasis. While these investigators were at work abroad, the first case, that of a European who had returned with Dr. Dutton in 1901, remained in Liverpool, and Dr. Annett infected monkeys and 25 per cent. of tame rats successfully, but did not succeed in infecting tame mice, rabbits or guinea-pigs. One of the infected monkeys died, but the other recovered, and no parasites

* For the history of the discovery see Boyce, Ross and Sherrington, *Lancet*, Feb. 21, 1903.

could be found by sub-inoculation into rats. The results of his work were incorporated in the report of the Expedition (*Memoir* XI). On reaching the Gambia, one thousand and forty-three natives were examined, the majority of whom were children or young adults, and apparently healthy; six were found to be infected. Trypanosomes were also found in the blood of a quadroon. Clinical descriptions were furnished in the report of these first eight cases of trypanosomiasis, of which those of the European and the quadroon terminated fatally after a duration of about eighteen months. Of thirty-six horses examined, ten were found to be infected with trypanosomes. Transmission experiments were made with *Glossina palpalis* and later with *Stomoxys*, but with negative results. A series of inoculations were made of the human and equine trypanosomes in experimental animals, the results of which led Dutton and Todd to the conclusion that the parasites were not of the same species; the Gambian horse trypanosome was subsequently named *T. dimorphon*. Several new species of flagellates occurring in birds, mice, tortoises, etc., were described in this report, including *T. johnstoni*, *T. mega* and *T. karyzeukton*.

Prior to the return of this Expedition, the discovery of trypanosomes in the cerebro-spinal fluid of cases of sleeping sickness in Uganda by members of the Sleeping Sickness Commission of the Royal Society, caused the subject of trypanosomiasis to assume great importance. At the invitation of King Leopold, an Expedition was sent in 1903 to study sleeping sickness in the Congo Free State, consisting of Drs. Dutton, Todd and Christy. The results of these investigations were incorporated in *Memoir* XIII, and illustrated the occurrence and distribution of trypanosomiasis, described the symptoms of the disease in all its stages, both in Europeans and natives, and showed how sleeping sickness, so-called, is related to trypanosomiasis as a symptom of that disease.

They first stated that they were unable to find any difference between the trypanosome occurring in cases of sleeping sickness in the Congo and *T. gambiense*. There was a very evident clinical connection between cases with only very slight symptoms (trypanosoma fever) and advanced cases of 'sleeping sickness.' In twenty-five of thirty-eight cases they found parasites in the cerebro-spinal fluid, adopting Quincke's new method of diagnosis by lumbar

puncture. They infected rats, mice, rabbits, guinea-pigs, and studied the morphology of the Congo and Gambian trypanosome in these animals. They noted that about 50 per cent. of such inoculations failed, and that they did not succeed in infecting two dog-face monkeys (*Cynocephalus* species).

In the combined areas of Leopoldville, Boma, Matadi and the Cataract Region, among a total of 1,172 persons examined, 8·8 per cent. were infected, while of these latter 55 per cent. had been diagnosed as cases of sleeping sickness. In the Gambia, the previous Expedition had examined 1,043 natives, of which six only harboured trypanosomes, and showed no definite symptoms.

Numerous lumbar punctures were made, and it was noted that in many cases the trypanosomes never find their way into the cerebro-spinal fluid, and in those cases in which they do they are more likely to be found towards the termination of the disease; if they gain access early in the disease, mania and other cerebral symptoms are more likely to be prominent, but their entrance is in no way correlated to the commencement of the fever or other symptoms. In two later papers (*Memoir* XVI, p. 97, and *Memoir* XVIII, p. 1) on gland puncture in trypanosomiasis, the observers favourably compared this with other methods of demonstrating the presence of parasites. Following the work of Greig and Gray, they concluded that by gland puncture, cases infected with trypanosomes could be recognised at a much earlier period than hitherto. They also, for the first time, observed a phenomenon frequently seen in cases of trypanosomiasis, namely, auto-agglutination of the red cells. The distribution of sleeping sickness in the Congo was subsequently studied (*Memoir* XVIII), it being concluded that the increase during recent years was due, in a great measure, to the increase in travel following the opening up of the country. In a subsequent report (*Annals*, Vol. I, p. 233), the trypanosomiasis of cattle was dealt with. The investigators found that this disease was very widely distributed in the Congo, the infecting parasite being usually *T. dimorphon*. It was also observed that domestic animals probably acquire a relative immunity to some strains of trypanosomes, and may even recover spontaneously. Trypanosomes were found in horses, mules and donkeys as well as in cattle, and also in *Tragelaphus scriptus*.

ENTRANCE HALL

Thomas, assisted by Linton and Breinl (*Memoirs* XIII and XIV), established by a long series of experiments that trypanosomes found in (*a*) the cerebro-spinal fluid of Uganda sleeping sickness cases, (*b*) the cerebro-spinal fluid and blood of Congo sleeping sickness cases, (*c*) the blood of Congo 'trypanosome fever' cases, and (*d*) the blood of Europeans infected in the Congo, were identical in animal reactions and morphology with *T. gambiense*, Dutton. It was also found (1) that the periodicity of the parasite is a prominent feature, both in man and beast; (2) that the passing of a strain from a susceptible into a very resistant animal does not attenuate the organism, and that the morphological character is retained after being passed through many hundreds of animals for nearly three years; (3) that the parasites in an animal may sometimes become more virulent, that such a strain may be particularly virulent for one species of animal, and that the more rapid infection is not due to the inoculation of a greater number of parasites than usual. In addition to *T. gambiense* and *T. dimorphon*, other pathogenic trypanosomes were procured, and comparisons made between the above organisms and *T. evansi*, *T. brucei*, *T. equinum* and *T. equiperdum*. Cultivation of the different parasites was also undertaken with success. Breinl gave a detailed account of the post-mortem changes in four cases of sleeping sickness (*Memoir* XVI).

Extensive research was conducted into the treatment of trypanosomiasis, with the result that two drugs only were found to be of any value in the disease, namely, arsenic and 'Trypanroth'. Thomas introduced atoxyl, a meta-arsenic anilin compound, a drug which causes no pain on sub-cutaneous injection and may be administered over a period of many months. He stated that it was 'the only remedy at present giving a prospect of a cure.' Although atoxyl would almost invariably cause the trypanosomes to disappear from the peripheral blood yet since the parasites frequently reappeared, it seemed possible that they might exist somewhere else in the body of their host in a form uninfluenced by the drug. Series of experiments were, therefore, undertaken by Benjamin Moore and Nierenstein, of the Bio-Chemical Department, and Todd. They found that in the treatment of rats infected with *T. brucei* the administration of atoxyl, followed by bi-chloride of mercury, gave better results than treatment by atoxyl alone.

Moore, Nierenstein and Todd, continuing their researches on the treatment of experimental trypanosomiasis (*Annals*, Vol. II, p. 265), found that in small animals, such as rats and rabbits, infected with *T. brucei*, the results of treatment by atoxyl followed by mercury salts were far superior to treatment by atoxyl alone; in large animals, as donkeys, on the other hand, the combined treatment was not found to be efficacious enough to be of practical value. These workers also studied the effects of therapeutic agents on trypanosomes in respect to (*a*) acquired resistance of the parasites to the drug, and (*b*) changes in virulence of the strains after escape from the drug (*ibid.*, p. 221). Further bio-chemical research into the subject was made by Nierenstein, who observed the acidity and alkalinity of the blood in trypanosome infections, and found that whereas the total acidity of the blood serum showed a marked increase, the total alkalinity remained constant (*ibid.*, p. 227). Later he made an extensive study of the chemo-therapeutics of atoxyl (*ibid.*, pp. 249, 323 and 329). Breinl conducted some experiments on the combined atoxyl-mercury treatment of monkeys infected with *T. gambiense* (*ibid.*, p. 345), and demonstrated that in five cases out of six, the administration of acetylated atoxyl and sublimate, and Donovan's solution, to monkeys (*Cercopithecus callithricus*), effected a complete cure. As the result of Plimmer and Thomson's discovery of the trypanocidal action of antimony, Breinl and Nierenstein investigated the action of aryl-stibinic acids in experimental trypanosomasis (*ibid.*, p. 365), and showed that both *p.* and *m.* amino-phenyl-stibinic acids are fairly powerful trypanocides, the former being superior in its action. Owing to the satisfactory results obtained in laboratory animals, a trial of the former compound in sleeping sickness patients was advised, the dose suggested being the same as for atoxyl.

In May, 1907, the Eighteenth Expedition of the School, consisting of Dr. Allan Kinghorn and Mr. R. E. Montgomery, was despatched to Rhodesia and British Central Africa to study the trypanosomiases of men and animals (*Annals*, Vol. II, pp. 53, 97, 333 and 387; Vol. III, pp. 259, 277 and 311). It was found that sleeping sickness had already invaded N.E. Rhodesia, the first case being seen in the Luapula division, adjoining the frontier of the Congo. Glossina surveys were made, and the suggestion first

advanced that *Gl. palpalis* and *Gl. fusca* were not the only transmittors of the disease, *Gl. morsitans* having also been observed in infected areas. Gland palpations were made in 26,928 natives, of whom 17·05 per cent. were found to have palpable glands. The percentage of positive punctures was 77·7. The workers confirmed the belief of Dutton and Todd that gland palpation, combined with puncture, is a most useful measure, being a practical method of isolating infected natives, and preventing any rapid extension of the disease. It was found that there were between fifty and sixty known cases of sleeping sickness in the country. The mode of introduction and prophylaxis of the disease were studied, and regulations drawn up by this Expedition were adopted and enforced by the Government.

Concurrently with the research into human trypanosomiasis, the Expedition pursued an enquiry into trypanosomiasis of domestic stock in North-Western Rhodesia, in the course of which it was established that the disease was very prevalent in that area, and was due to *T. dimorphon*, *T. vivax* and a trypanosome morphologically allied to *T. brucei*. These trypanosomes could be transmitted by *Gl. morsitans*, by *Stomoxys calcitrans* and by a species of *Lyperosia*. The question of association of big game and *Gl. morsitans* was considered, the opinion being that the distribution of *Gl. morsitans* is entirely dependent upon the nature of the country and its flora, that the association with the fauna is largely fortuitous, and that a perpetual supply of mammalian blood is not imperative, at least to its temporary existence.

The classification of trypanosomes was attempted, the observers dividing the thirteen named species in the following way:—*T. theileri*, *T. equinum*, *T. gambiense* and *T. equiperdum*, easily recognised by their morphology or animal reactions; the nine remaining species sub-divided into three groups having as their types:—(1) *T. evansi* (with *T. brucei* and *T. sudanense*). (2) *T. dimorphon* (with *T. congolense* and *T. pecaudi*, and (3) *T. nanum* (with *T. vivax* and *T. cazalboui*).

Research was undertaken into many other points, and included observations on the parasites occurring in the intestine of *Gl. palpalis* and in the intestine and proboscis of *Gl. morsitans*.

The many problems of trypanosomiasis continued to occupy the

energies of the staff at Runcorn. Yorke took up the study of immunity in trypanosome diseases. He was able to prove (*Annals*, Vol. III, p. 565) that a diminution of the haemolytic complement only takes place in the last stages of the disease, and that, in an experimental case, the complement had practically vanished shortly before the death of the animal, when the blood was swarming with parasites. He also worked on the protective action of the serum of animals in a state of chronic infection or immune to various kinds of trypanosomes. Later, he investigated the condition of the blood which gives rise to the phenomenon of auto-agglutination of the red blood cells in animals infected with trypanosomes and to sleeping sickness in man (*Proc. Roy. Soc.*, Ser. B, Vol. LXXXIII, p. 238, and *Annals*, Vol. IV, p. 529). Experiments showed that auto-, iso- and hetero-agglutinin exist in the blood of many normal animals, and are frequently present in much greater amount in the blood of infected animals. Apart from infection with trypanosomes, well marked auto-agglutination was found to be an extremely rare phenomenon. Ross and Thomson studied a case of sleeping sickness and demonstrated a regular periodical increase of the parasites (*Annals*, Vol. IV, pp. 261 and 395). These workers confirmed the claim that there is a life cycle of trypanosomes in the vertebrate host (*ibid.*, p. 465). In 1910, Stephens observed a marked peculiarity in the morphology of a trypanosome from a rat supposed to be infected with *T. gambiense*. This parasite was described by himself and Fantham (*Annals*, Vol. IV, p. 343), the animal reactions observed by Yorke (*ibid.*, pp. 351 and 385), and a new species was founded, to which the name *T. rhodesiense* Stephens and Fantham was given, based on the peculiar posterior position of the macronucleus. It was later established that *T. brucei* exhibits this peculiarity.

In 1911, the Twenty-seventh Expedition of the School, consisting of Dr. J. L. Todd and Dr. S. B. Wolbach, was despatched to the Gambia to investigate sleeping sickness. Reports of the work done were published in the *Annals*, Vol. V, p. 245.

In the course of this investigation, 12,298 persons were palpated, and the observers put on record their opinion that gland palpation and puncture was by far the best procedure for the diagnosis of trypanosomiasis. It was found that at least 0·8 per cent. of the

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population of the Gambia was infected with trypanosomes. Strong recommendations were made for the control of the disease in the Gambia, including a continued examination of the whole population, the establishment of villages for isolation, observation and treatment of cases, and the appointment of a special staff for the administration and execution of these projects. Stannus and Yorke examined in rats the parasite from a case of sleeping sickness contracted in Nyasaland (*ibid.*, p. 443), and were convinced that the trypanosome in question was not *T. gambiense* but probably identical with *T. rhodesiense*, which it resembled very closely, having a posterior nuclear form. A study was made by Yorke and Blacklock of the trypanosomes from a horse naturally infected in the Gambia (*ibid.*, p. 413). The parasites consisted of a long form with a free flagellum, and also a short form without a free flagellum. The former was considered, from its morphological appearance and animal reactions, to belong to the *T. vivax* group; the latter form was subsequently identified (*Annals*, Vol. VI, p. 107) as *T. dimorphon*, sensu Laveran and Mesnil. Blacklock measured one thousand examples of this form, and found that the average length was 13·3μ (*Annals*, Vol. VI, p. 287). Measurements of one thousand examples of *T. vivax* in goats were made by Blacklock, the average length being 27·7μ (*Annals*, Vol. V, p. 521). He also, using the same strain of *T. vivax*, measured fifty trypanosomes drawn from a rat and a rabbit respectively. In the former the average length was 21·1μ, in the latter 20·8μ (*ibid.*, p. 537).

In 1911, at the request of the British South African Co., Dr. Kinghorn and Dr. Yorke were sent to Rhodesia (Luangwa Valley) to study sleeping sickness. It was quickly placed beyond doubt that *Gl. morsitans* was the carrier of the human trypanosome (*Annals*, Vol. VI, p. 1). The investigators inoculated rats from twelve cases of human trypanosomiasis, eleven of which occurred in villages in the Luangwa valley. In every instance they observed the posterior displacement of the macronucleus, characteristic of the trypanosome described by Stephens and Fantham; the animal reactions agreed in all respects with those obtained from infection with *T. rhodesiense*. Elaborate transmission experiments with both wild and laboratory-bred *Glossina morsitans* were successfully carried out in rats and monkeys; the duration of the cycle in the

fly (approximately fourteen days) was found to be shorter than in experiments of previous investigators with *Gl. palpalis* and *Gl. morsitans*. It was observed that an infected fly retains the power of transmitting the disease during its life, and is infective at each meal, but that mechanical transmission does not occur if a period of twenty-four hours has elapsed since the infecting meal. Certain species of buck, viz., waterbuck, hartebeest, mpala and warthog, were found to be infected with the human trypanosome, as well as a native dog. Later (*Annals*, Vol. VI, p. 269), it was found that 16 per cent. of the local game were infected with *T. rhodesiense*, and it was established that the game and fly strains were identical with the human trypanosome. In all, six species of tryanosomes were found in game and domestic stock in the Luangwa Valley (*Annals*, Vol. VI, p. 301), namely, *T. rhodesiense* and *T. pecorum*, transmitted by *Gl. morsitans* and probably by insects other than tsetse-flies; *T. vivax* and *T. nanum*, probably transmitted by *Gl. morsitans;* and two others, one of which was possibly *T. montgomeri*. At least 37·5 per cent. of the buck were found to harbour pathogenic trypanosomes. In a later report (*ibid*, p. 317) a new trypanosome, *T. ignotum*, infective to monkeys and a rabbit, was described. The vertebrate host was not discovered. This trypanosome is now known as *T. simiae*, having been previously found in the same year by the Royal Society S.S. Commission. Still later (*Annals*, Vol. VII, p. 254), descriptions were given of *T. multiforme*, sp. n., and of *T. tragelaphi*, the latter closely resembling *T. ingens*. In the course of experiments in the development of *T. rhodesiense* in *Gl. morsitans* (*Annals*, Vol. VI, p. 405), it was observed that the cycle was influenced to a marked degree by the temperature to which the flies were subjected, high temperatures (75° to 85° F.) being favourable and low ones (60° to 70° F.) unfavourable to the development of the parasites. Parasites might persist in the fly at at incomplete stage of their development for at least sixty days under unfavourable climatic conditions. It was found (*Annals*, Vol. VI, p. 495) that in every fly capable of infecting animals with *T. rhodesiense* the salivary glands were invaded, also that on every occasion on which the salivary glands were infective the trypanosomes in the intestines were virulent. Invasion of the salivary glands was only observed

in the case of flies infected with *T. rhodesiense* and not in the case of any other trypanosomes met with in the Luangwa Valley or on the Congo-Zambesi watershed. It was calculated that approximately 3·5 per cent. of the flies might become permanently infected and capable of transmitting the virus (*Annals*, Vol. VII, p. 183). The chief reservoir of the human trypanosome was found to be the antelope. Stephens and Fantham (*Proc. Roy. Soc.*, B, Vol. LXXXV, p. 223, and *Annals*, Vol. VI, p. 131) made a bionomic study of *T. rhodesiense*. One thousand specimens were measured, and it was found that the average length was 23·6μ, as compared with *T. gambiense* 22·1μ, and *T. brucei* 23·2μ. The average length of *T. rhodesiense* in man and other species of animals was ascertained. Those in the rat were found to be the longest (24·5μ) and those in the rabbit the shortest (19·4μ). Of the three species *T. rhodesiense* was found to be richest in long and poorest in intermediate forms. Another series of measurements was undertaken (*Annals*, Vol. VII, p. 27), when each day, for the first ten days of infection, one hundred trypanosomes from the same rat were measured, the results being again compared with *T. gambiense*. It was found that the day of infection was of great importance, as there was a great variation in the percentage of 'stumpy' forms on different days, *e.g.*, 53 per cent. on the seventh day to 5 per cent. on the tenth day. The larger the sample of trypanosomes taken, the smaller the variation in the average length.

J. G. Thomson succeeded in cultivating *T. rhodesiense* by the use of a modification of the Novy-MacNeal-Nicolle medium. The changes taking place in the trypanosomes were described (*Annals*, Vol. VI, p. 103), and it was noted that when development was rapid two distinct types could be distinguished on the fourth day. In cultures which develope more slowly the trypanosomes disappeared about the third or fourth day, reappearing about the sixth, and on the eighth day spirillar forms were seen to be splitting off. Differentiation into the so-called 'male' and 'female' forms took place during the eighth, ninth and tenth days. Inoculation of animals from the cultures was unsuccessful. In a subsequent investigation with J. A. Sinton (*ibid.*, p. 331), Thomson successfully cultivated *T. gambiense* as well as *T. rhodesiense*, the former for a period of thirty-seven days, the latter for twenty-one

days only. The life history of these trypanosomes in culture tubes was similar to that occurring in the gut of the insect host. The cultures lost their infectivity after the third day, and it was suggested that probably their transference to a new medium or environment similar to that of the salivary glands of the tsetse fly might be required to permit the full history of the trypanosomes being completed. Blacklock observed the vitality and changes undergone by trypanosomes in the cadaver of the animal host (*ibid.*, p. 55): He found that *T. gambiense* and *T. rhodesiense* can remain infective in the blood of the dead animal for forty-eight hours. Blacklock also made a study of the posterior nuclear forms of *T. rhodesiense* in rats (*Annals*, Vol. VII, p. 101). He found that they first appeared in the blood from the sixth to the tenth day of the disease, in a count of a thousand trypanosomes, that they increased in numbers in the later stage of the disease, and that they increased relatively to other forms of trypanosomes. They showed definite powers of resistance to disintegration in the cadaver of the animal host. It was suggested that such forms might occur as a constant constituent of certain strains.

Stephens and Blacklock made a morphological study of *T. brucei* (the Zululand strain) and of the trypanosome of the same name from the Uganda ox (*Annals*, Vol. VII, p. 303). They asserted the non-identity of the two strains, and proposed for the latter the name *T. ugandae*. Blacklock and Yorke (*ibid.*, p. 603), studying the pathogenicity of *T. congolense* (Broden) and *T. nanum* (Laveran), came to the conclusion that they were the same parasite.

Yorke and Blacklock studied the characters of the more important mammalian trypanosomes (*Annals*, Vol. VIII, p. 1), and compiled a convenient table of the main differential points. The value of the cycle of the trypanosomes in their invertebrate hosts as an aid to differentiation of species was also put forward.

Todd re-examined the flagellate found by Dutton in 1902 in the blood of Gambia house mice, and came to the conclusion that it was *T. acomys* (*ibid.*, p. 469).

Yorke and Blacklock experimented with antimony trioxide in the treatment of experimental trypanosomiasis (*ibid.*, p. 55), controlling and extending some of the work of Kolle and others on the use of this drug. Various strains were used in the experiments.

LECTURE THEATRE

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It was found that small animals could withstand a relatively much larger quantity of the drug than large ones. Post-mortem evidence proved that the proportion absorbed during a period of six months was exceedingly small. A certain number of cures would seem to have resulted, as several animals remained negative without relapse for over two hundred days, and sub-inoculated animals were not infected. Most strains appeared very susceptible to the drug, but *T. gambiense* and *T. lewisi* proved refractory.

Seidelin tested the effect of salvarsan-copper on white rats infected with a strain of trypanosomes of the *T. brucei* group kept in guinea-pigs and rats in West Africa (*Annals*, Vol. IX, p. 197). The best results were obtained with the injection of a dose of 0·0064 gm.; in such a case the trypanosomes disappeared from the blood on the following day and remained absent for fifteen days, death occurring on the twenty-eighth day; in several other cases the life of the animals was prolonged for a few days more.

The Thirty-second Expedition of the School, consisting of Drs. Yorke and Blacklock, was despatched to Sierra Leone in 1914. Research was undertaken into the bionomics of *G. palpalis* in Sierra Leone, with special reference to its pupal habits (*Annals*, Vol. IX, p. 249). It was found that the breeding-grounds of *G. palpalis* are not so strictly limited to the immediate vicinity of water as had hitherto been believed. Mangrove swamps do not constitute a breeding-ground. The pupae do not hatch when subjected to daily flotation on sea water. The ground around the trunk of oil palms which have not been stripped of their lower petioles constitutes an excellent breeding-place for *G. palpalis*; they can breed in localities in which practically the only tree is the oil palm. A study of the food of *G. palpalis* in the Cape Lighthouse Peninsula, Sierra Leone (*ibid.*, p. 363), showed that about 8 per cent. of the wild *G. palpalis* in that district contained recognisable red blood cells—7 per cent. of mammalian origin and 1 per cent. nucleated red cells of unknown origin. Neither shed blood nor other fluid which is exposed (not covered by a membrane) can be imbibed by *G. palpalis*. Fluids such as solutions of sugar, sodium chloride, etc., protected by a membrane (*e.g.*, thin rubber sheeting), were taken up, but less quickly and readily than blood. It was thought that in nature *G. palpalis* may, under certain conditions, take up fluids other than

blood. The human trypanosome (*T. gambiense*) was discovered in an ox in Sierra Leone (*ibid.*, p. 383), thus demonstrating that domestic stock forms a reservoir for the virus of sleeping sickness. Among other animal parasites found in domestic stock in Sierra Leone (*ibid.*, p. 413), *T. congolense* and *T. vivax* were most commonly encountered. Trypanosomiasis of cattle was common. Of one hundred and forty-three examined, trypanosomes were found in nineteen after a single examination.

In 1919, Escomel recorded the discovery of trypanosomes in the blood of a patient coming from Peru, which he described and considered to be *Schizotrypanum cruzi*. Yorke, examining this description, was led to doubt, on morphological grounds, whether the identification was correct, and proposed for this Peruvian parasite the name *T. escomeli*, in recognition of its discoverer. A feature of the symptomatology of the case was the overpowering somnolence from which the patient suffered, a symptom not hitherto noted in Chagas' disease, although a striking feature of the African trypanosomiasis of man (*Annals*, Vol. XIII, p. 459).

Macfie described a trypanosome found in the blood of a snake, *Naja nigricollis*, in the Gold Coast, resembling in some degree *T. primeti*, but differing from it in size and proportion. He proposed for it the name *T. voltariae* (*Annals*, Vol. XIII, p. 23).

YELLOW FEVER

In 1900, the Fourth Expedition, consisting of Drs. H. E. Durham and Walter Myers, went to Brazil to study yellow fever. Dr. Myers died of the disease in January, 1901, while Dr. Durham, who also contracted it, recovered and published a report of the work of the Expedition (*Memoir* VII) in 1902.

The U.S. Yellow Fever Commission in Cuba had not yet established the transmission by *Stegomyia* when the Liverpool Expedition set to work at Pará; for which reason the course of their investigation was chiefly directed at first to the search for some protozoal parasite. Only seventeen autopsies on yellow fever cadavers were obtainable. An extremely slender filiform bacillus was observed to occur constantly in the tissues and intestines, and much time was spent in isolating it and in attempts at cultivation.

Dissection of specimens of *Culex fatigans* captured in suspected houses showed large numbers of a similar bacillus. Owing to the death of Dr. Myers, the research came to an end.

In 1905, Professor Rubert Boyce was despatched by the School to New Orleans, to observe the work of the U.S. Medical Authorities in dealing with the outbreak of yellow fever there. In *Memoir* XIX Boyce gave an account of the vigorous campaign which was successful in ridding the city of *Stegomyia*. Subsequently, at the request of the Colonial Office he visited Honduras to make a report on the conditions existing in that Colony with reference to a recent outbreak of yellow fever (Waterlow & Sons, 1906).

In April, 1905, a second Yellow Fever Expedition was sent to the Amazon, the members being Dr. Wolferstan Thomas and Dr. Breinl. A permanent laboratory was established so that patients could be kept under continued observation, and experiments inaugurated which would have been impossible under other conditions. Series of reports by Thomas were published in the *Annals*, Vol. IV, p. 1. It was recorded that the most serious disease to which the foreign population was liable was yellow fever, and this disease was made the object of extensive investigation. 'Chimpanzees have been successfully inoculated; rabbits and guinea-pigs exhibited certain reactions when inoculated with infective blood from yellow fever cases or subjected to the bites of infected *S. calopus*.' (See also *Trans. Soc. Trop. Med. and Hyg.*, Vol. III, p. 59.) The resources of the laboratory in Manãos were placed at the disposal of the State, the doctors, the hospital and the poor of the city. Examinations of blood, agglutination reactions for typhoid and paratyphoid, bacteriological examinations of water and milk, post-mortems and pathological reports were made, and the laboratory so conducted as to be of the greatest possible service to the community. Papers on 'Oesophagostomiasis in Man' and the condition known as 'Mossy Foot' were published in the *Annals*, as also an article on the 'Mosquitoes of the Amazon region' by Newstead jointly with Thomas.

In 1910, at the request of the Colonial Office, Professor Boyce was despatched to the Gold Coast and Sierra Leone, to report on the outbreak of yellow fever at those places (*Trans. Soc. Trop. Med. and Hyg.*, Vol. IV, p. 33). It was observed that the so-called

classical type of yellow fever was comparatively rare amongst native races, and the reason was advanced that natives are partially immunised by being born and brought up in an endemic area (*Annals*, Vol. V, p. 103). Those removed in childhood from such an area become non-immune, and therefore liable to succumb to an epidemic.

In 1911, the study of yellow fever was taken up with energy by Professor Boyce, who suggested and superintended the establishment of a Yellow Fever Bureau at the Liverpool laboratories. A *Bulletin* was issued, in which the Director of the Bureau, Dr. Harald Seidelin, and other investigators published the results of their researches. Abstracts of reports from all over the world were also made, and reviews published of current literature on yellow fever and allied subjects, including pappataci fever and dengue. Research was undertaken into the etiology, diagnosis and treatment of yellow fever. Seidelin observed the occurrence of protozoon-like bodies in the blood and organs of yellow fever patients (*Journ. Path. and Bact.*, Vol. XV, p. 282). At a meeting of the Society of Tropical Medicine and Hygiene, in January, 1911, these organisms were demonstrated in preparations of the blood and sections of the kidney, and later (*Yellow Fever Bulletin*, Vol. I, p. 229), Seidelin described their morphology, and proposed for them the name of *Paraplasma flavigenum*, g. n., sp. n. In December, 1911, he was despatched to Yucatan, where an epidemic of yellow fever was raging; a report of this Expedition was published in *Yellow Fever Bull.*, Vol. II., p. 123. The total number of cases officially diagnosed during the outbreak was seventy-three, with thirty-eight deaths. The existence of a 'microbe carrier' was put forward as being responsible for the maintenance of the virus during periods when the disease is latent, it being suggested that the fragile infected *Stegomyia* could not be the lasting reservoir. It was also considered that one attack does not necessarily confer immunity. The usually mild form of the disease in natives was said to be due either to an unrecognised infection in childhood or to the hereditary transmission of anti-bodies from immune parents. Clinical features of the cases observed were given. *Paraplasma flavigenum* was seen in fifteen confirmed cases of yellow fever out of sixteen examined. Summing up the results of his blood examinations for *P. flavigenum*

MUSEUM

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in undoubted cases of yellow fever, Seidelin found that on this and former occasions he had approximately one hundred and six positive cases out of a total of one hundred and twenty. Records were made of the examination of four hundred and twenty-one specimens as controls. In one hundred and thirty-six cases malarial parasites were found, and in two hundred and eighty-three no parasites at all, while in two young children under no suspicion of yellow fever *P. flavigenum* occurred. It was suggested that these, together with two others previously observed, might be 'microbe carriers.' Blood from yellow fever cases was inoculated into four guinea-pigs, but none showed symptoms resembling the disease. A mosquito survey of Merida was made, and recommendations advanced as to methods of extermination. A section of Seidelin's report was devoted to a reply to those who had criticised his work.

In 1915, the Yellow Fever Commission (West Africa) concluded that no proof had been given that *P. flavigenum* was of a protozoal nature, and that the nature of the virus of yellow fever still remained undetermined.

In December, 1912, Seidelin was sent to Jamaica in order to investigate the nature of the disease called 'vomiting sickness,' prevalent in that island during the winter months, and responsible for a considerable mortality, chiefly among native children. A report of this Expedition was published in the *Annals* (Vol. VII, p. 377) and also in the *Yellow Fever Bulletin* (Vol. III, p. 7). Sixty-two cases were observed, but no causal organism was recognised; it was concluded that 'vomiting sickness' was a local disease and could not be accepted as a form of meningitis, which view had been advanced by Scott two years before the latter's demonstration of its true origin.

RELAPSING FEVER AND SPIROCHAETES

By the death of Dr. Dutton from tick fever while serving with the Congo Expedition, the School suffered the loss of one of its most brilliant workers, who, although only twenty-nine years of age, had already won a recognised position throughout the scientific world. Towards the end of 1904, Dr. Dutton and Dr. Todd had reached Stanley Falls, and they were able to demonstrate independently the

cause of tick fever in man, a discovery made a few weeks previously by Ross and Milne in Uganda. Further, they were able to prove the transference of the disease from man to monkeys by means of a particular species of tick. In Todd's report of this discovery (*Memoir* XVIII) clinical descriptions were given of twelve native and two European cases (the last two being those of the investigators themselves), all of whom were infected with a spirochaete thought at first to be *S. obermeieri*. A number of inoculation experiments with laboratory animals were carried out, it being found that to monkeys alone the parasite appeared to be uniformly pathogenic. Observations were made upon the distribution and bionomics of the human tick in the Congo, and included in the report was a description of *Ornithodoros moubata* by Professor Newstead.

Research was proceeding at Runcorn upon material brought back from the Congo by Dr. Todd. Dr. Breinl, invalided home from the Fifteenth Expedition, carried out with Dr. A. Kinghorn extensive studies on 'tick fever' and 'relapsing fever.' Observations were made on the animal reactions of the spirochaete discovered in the Congo cases of human tick fever, and brought to England in infected monkeys and ticks. In the course of these experiments, infection was produced not only in monkeys, but also in a horse, a dog, rabbits, guinea-pigs, rats and mice. This fact caused the observers to conclude that the organism was distinct from *Spirochaeta obermeieri*, pathogenic hitherto to monkeys only. Further experiments were undertaken, confirming this conclusion; and the new species was given the name of *Spirochaeta duttoni* (Breinl and Kinghorn, 1906, *Memoir* XX). Studies were made of this organism (*Memoir* XXI), in the course of which a clinical comparison was made between African tick fever and European relapsing fever, and the research into the animal reactions of this spirochaete in various animals amplified and completed. Experiments in immunity were continued, the conclusions reached being: (1) In animals which have recovered from the infection there is a relatively active immunity of comparatively long duration; (2) immune serum cannot produce passive immunity, nor has it any curative action; (3) hyper-immune serum does not protect a susceptible animal, nor does it prevent relapse, but it mitigates the severity of the infection and occasionally cuts short an attack; (4) there is a slight inborn immunity of short

duration. It was also shown that *S. duttoni* may pass *in utero* from mother to foetus, and extensive studies were carried out to determine the rôle played by the spleen in infection by spirochaetes. Attempts were made to transmit spirochaetes by the bites of *Cimex lectularius*, but without success. Subsequently (*Annals*, Vol. I, p. 435) Breinl studied the morphology and life history of *S. duttoni*, while Markham Carter (*ibid.*, p. 15) described the multiplication and important changes in form of *S. duttoni* in eggs laid by infected ticks. Still later (*Annals*, Vol. V, p. 479), Fantham studied the life cycle of spirochaetes, amongst those considered being *S. duttoni*, *S. recurrentis* and *S. marchouxi*. Subsequently (*Annals*, Vol. VIII, p. 471) he investigated the granule phase of the parasite, a detailed study being given, while serving with the Expedition to Khartoum, to *S. bronchialis*, in which it was found that the granules formed by the spirochaete were the cross infective stages of the organism (*Annals*, Vol. IX, p. 391).

In 1917, while making microscopical examinations of stained smears from the stools of five hundred and fifty-four patients, admitted to hospital for dysentery, Carter found that 56·5 per cent. were infected with *Spirochaeta eurygyrata*. A control investigation on one hundred cases free from intestinal disorders showed 41 per cent. to be infected (*Annals*, Vol. X, p. 391). Repeating this investigation amongst a normal population, Macfie and Carter (*Annals*, Vol. XI, p. 75) examined eighty-two hospital patients suffering from some surgical condition, and twenty-three normal healthy men. None of the cases had ever resided in the tropics. Of the hospital patients 56·2 per cent., and of the healthy men 43·8 per cent., harboured *S. eurygyrata*. A second species of spirochaete was discovered in the intestine of one case, which, owing to its larger size and certain morphological peculiarities, was considered to be a new species, and named by them *Spirochaeta intestinalis*. Macfie and Yorke examined the morphology of the spirochaetes responsible for European, African and Indian relapsing fevers (*Annals*, Vol. XI, p. 81), and reached the conclusion that there is at present no means of distinguishing these parasites morphologically.

AMOEBIASIS

Research into the amoebae parasitic in the human intestine was undertaken by Fantham, and a study commenced of the life history of *E. coli* as seen in cultures (*Annals*, Vol. V, p. 111).

Carter, Mackinnon, Matthews and Smith conducted extensive researches into the protozoal findings in cases of amoebic dysentery. In their first report (*Annals*, Vol. X, p. 411) they recorded the results of four thousand three hundred and thirty-four examinations of nine hundred and ten patients suffering from this condition. Protozoal infections were discovered in 44·2 per cent.; *E. histolytica* was found in 10·3 per cent. of the cases; *E. coli* in 25·4 per cent.; *G. intestinalis* in 18·6 per cent.; *T. intestinalis* in 1·2 per cent.; and *C. mesnili* in 2·7 per cent. Their second report (*Annals*, Vol. XI, p. 27) recorded similar examinations of one thousand seven hundred and thirteen cases of dysentery. Stress was laid upon the necessity for repeated examinations of each patient, as cases found negative the first and second times may prove on further examination to be *E. histolytica* carriers. The subject of 'negative periods' (absence of vegetative forms and cysts) in infected cases was also dealt with. A third report of this investigation appeared in *Annals*, Vol. XIII, p. 83. Yorke and the above-mentioned observers examined for intestinal protozoa three hundred and forty-four persons who had never been out of England (*Annals*, Vol. XI, p. 87). Of this number, two hundred and six were healthy young men of about 18 years of age who had recently entered the Army. A single examination of each of these cases revealed the interesting fact that 3·9 per cent. were infected with *E. histolytica*. In an address to the British Medical Association (*B.M.J.*, April 12th, 1919), Yorke emphasized the importance of discovering whether the infection in this country is recent or otherwise. He was inclined to believe that it was not recent because (1) carriers must have frequently entered this country before the war; (2) all the necessary factors for the spread of the infection are to be found in this country; (3) there are authentic records of cases of amoebic dysentery and liver abscess before 1914.

Stephens and Mackinnon treated eighty-one cases infected with *E. histolytica* with 'alcresta ipecac,' an adsorption compound of

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emetine and aluminium silicate (*Annals*, Vol. X, p. 397), with the result that about two-thirds of the patients were freed from amoebic cysts. Carter and Matthews, using Cropper and Row's method of concentration (*Annals*, Vol. XI, p. 195), found *E. histolytica* cysts in five of one hundred and thirty-three apparently negative cases which had already received three ordinary routine microscopical examinations. Smith made a mensurative study of the cysts of *E. histolytica* and *E. coli* (*Annals*, Vol. XII, p. 27), and investigated the question of the number of races in the former parasite (*Annals*, Vol. XIII, p. 1). It was shown that not all infections of *E. histolytica* remain constant from one day to another in the average size of their cysts. The species can be divided into two races characterised by larger and smaller cysts, respectively. Infections with *E. histolytica* in healthy carriers who have never been out of England were shown to be characterised by a smaller proportion of the 'small' race, and also by a reduced proportion of the larger cysts of the 'ordinary' race, as compared with infections from convalescent dysenterics from abroad. Investigating the incidence of amoebic dysentery in asylum patients never out of England (*Annals*, Vol. XIII, p. 177), Smith found that of five hundred and four patients examined, fifty-nine had acute dysentery, and in three cases vegetative *E. histolytica* were found in the stools.

BERI-BERI

Simpson and Edie undertook research into the relation of the organic phosphorus content of various diets to diseases of nutrition, particularly beri-beri. After a review of the work of Schaumann and others (*Annals*, Vol. V, p. 313), the investigators recorded their own experiments with pigeons fed on various kinds of rice, white bread and whole-meal bread. A study was made of the anti-neuritic bases of vegetable origin in relationship to beri-beri, the properties of the yeast extracts investigated, and a method adopted for the isolation of torulin, the anti-neuritic base of yeast (*Annals*, Vol. VI, p. 235).

Stephens (*Thompson-Yates Lab. Reports*, Vol. VII, p. 9), described the morphology of *Gastrodiscus hominis*, of two new human cestodes, *Dibothriocephalus parvus* and *Taenia bremneri*, of a new linguatulid, *Porocephalus pattoni* (*Annals*, Vol. I, p. 549), and of a new human nematode, *Strongylus gibsoni* (*Annals*, Vol. II, p. 315). Observations on the hooklets of *Cysticercus cellulosae* in man (*Annals*, Vol. II, p. 391) showed that there is an irregularity of development affecting both the number of the hooklets and, more especially, the size. A fluke, found by Newstead in the alimentary canal of a Nicaraguan turtle, was described by Stephens (*Annals*, Vol. V, p. 497), who proposed for it a new genus and named it *Desmogonius desmogonius*. The fluke from the liver of native dogs at Kasauli, India, was separated by Stephens from the genus *Opisthorchis* owing to the existence of a process or pedicle bearing on its summit the genital opening and a ventral sucker, and placed in a new genus as *Paropisthorchis caninus* (*Annals*, Vol. VI, p. 117). Breinl and Hindle described a new *Porocephalus*, found in the lung of one of their experimental monkeys, and distinguished from the known species by the presence of an appendage on the outer pair of hooks only. They proposed for it the name of *Porocephalus cercopitheci* (*Annals*, Vol. II, p. 321). Dogs in Freetown were found by Yorke and Blacklock to be heavily infected with *Ankylostoma caninum* and *A. ceylanicum*, the species being present in about equal numbers (*Annals*, Vol. IX, p. 425).

In 1916, Stephens contributed the section on Helminths to 'The Animal Parasites of Man,' issued jointly with Fantham and Theobald.

In 1917, at a Veterinary Hospital attached to a remount depôt in the neighbourhood of Liverpool, Yorke and Macfie started an investigation into the parasitic worms causing a heavy mortality amongst horses recently imported from America. The parasites belonged for the most part to various genera of the family *Strongylidae*, and in the course of their study Yorke and Macfie described eight new species and one new variety, viz., *Cylicostomum longibursatum*, *C. minutum*, *C. pseudocatinatum*, *C. pateratum*, *C. tridentatum*, *C. triramosum*, *Cylindropharynx rhodesiense*,

Gyalocephalus equi and *Cylicostomum nassatum*, Looss, var. *parvum* (*Annals*, Vols. XI-XIV).

Yorke and Southwell described a nematode from the intestine of a zebra, which certain minute characters of the head, and also the position of the vulva, led them to regard as a new species, for which they proposed the name *Crossocephalus zebrae* (*Annals*, Vol. XIV, p. 127).

FILARIASIS

The second part (*Memoir* IV) of the Report of the Third Malarial Expedition was devoted almost entirely to Filariasis. Eight new species, found during the examination of a large number of West African birds, were described, namely:—*F. cypseli*, *F. spiralis avium*, *F. fusiformis avium*, *F. spiralis avium major*, *F. falciformis*, *F. bibulbosa*, *F. capsulata* and *F. shekletoni*. Observations were also made on human filariasis in West Africa, it being found that throughout the whole of that area the natives appeared to be infected with *F. nocturna*, *diurna* and *perstans*. With regard to the two first species, the majority of the cases encountered were atypical, in that, embryos were either never absent from the peripheral blood, or the maximum did not occur at mid-day and mid-night or thereabouts according to the species. Among the former cases there were many showing decided periodicity, and, among the latter, the hour at which the maximum number was present varied considerably. In some cases, two maxima during the twenty-four hours were indicated. In the examination (day blood) of three hundred and ninety natives of all ages up to about eighteen years, one case only, aged eleven years, was infected. The observers succeeded in infecting *A. costalis* (proboscis) with *F. nocturna*. They considered that the weight of evidence was on the side of the identity of *F. nocturna* and *F. diurna*, but that many points remained to be cleared up before the question could be settled.

A study of the periodicity of *Microfilaria nocturna* was made by Yorke and Blacklock (*Annals*, Vol. XI, p. 127). They found that obstruction to the passage of *M. bancrofti* through the cutaneous vessels occurs at all times of the day and night, but is at a minimum

at the end of the period of bodily activity. Although this obstruction aids in the piling up of the larvae in the cutaneous vessels, it is in no way responsible for the nocturnal periodicity, which is primarily dependent upon periodic variations in the arterial supply of larvae to the cutaneous vessels. By reversing the hours of sleep and activity, cutaneous immigration gradually becomes diurnal instead of nocturnal, the complete inversion of the periodicity being accomplished in from four to eleven days. The number of microfilariae, as judged from the maximum concentration in the cutaneous blood, remained at practically a constant level during the period of observation. The number of microfilariae in the urine varied greatly, the variation giving no indication of either a nocturnal or a diurnal periodicity. The number of microfilariae in the renal and vesical vessels exhibited a nocturnal periodicity analagous to that in the cutaneous vessels.

ENTOMOLOGY

In 1907, Professor Newstead, jointly with Drs. Dutton and Todd, issued a report (*Annals*, Vol. I, p. 1) upon the insects and other arthropoda collected in the Congo Free State. Among the new genera and species described and figured were *Eretmapodites inornatus*, *Stegomyia luteocephala*, *S. albomarginata*, *Duttonia tarsalis*, *D. africana*, *Culex laurenti*, *C. par*, *Mimomyia africana*, *M. malfeyti*, *Boycia mimomyiaformis*, *Haematopota duttoni*, *H. trimaculata*, *Tabanus billingtoni*, *Glossina maculata* and *Stomoxys omega*. The habits and structural characters of the larva of *Simulium ornatum* (a European species) were described. They occur on the under sides of submerged leaves or blades of grass in those parts of a stream which are rapidly flowing and fully exposed to the sun. Their mode of progression resembles that of looper caterpillars, spinning a network of silken threads along which they travel. The period of pupation varies from two to six days. The imagines escape through a slit in the thorax, and occasionally may be seen completely immersed in water with their wings folded so as to encase an air bubble. The distribution of tsetse-flies in the Congo was recorded and illustrated by a map, together with observations on the bionomics of the flies. The life history of *Stomoxys calcitrans* was also described in detail.

ENTOMOLOGICAL DEPARTMENT

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In the following year, Newstead made a study of the bionomics of the common house-fly (*Annals*, Vol. I, p. 507). The chief breeding-places were determined, and it was established that the life-cycle of the fly, in all kinds of fermenting material, is reduced to the minimum period of ten to fourteen days; and that in the absence of such artificial heat the cycle may occupy a period from three to five weeks or more, according to the temperature of the outside air. It was found that house-flies do not depend entirely upon excessively warm weather for breeding purposes. Methods of prevention were suggested, and some notes appended on other insects found during the investigation.

In 1908, Newstead went to Jamaica to study cattle ticks. In the course of the investigation, twenty-five estates were visited and the cattle inspected in each, and large numbers of ticks were collected in every district (*Annals*, Vol. III, p. 421). Methods of treating tick-infected stock were made the subject of enquiry, and whenever possible practical demonstrations were given. The nature and extent of injury caused by insects and other pests to cultivated crops was studied, and methods of control advised. Descriptions were given of the nine species of ticks found in Jamaica, namely, *Argas persicus*, *Margaropus annulatus australis*, *Rhipicephalus bursa*, *R. sanguineus*, *Dermacentor nitens*, *Amblyomma maculatum*, *A. cajanense*, *A. dissimile*, *Aponomma* sp.

In 1906, Newstead investigated the life history of *Stomoxys calcitrans* (*Journ. Econ. Biol.*, Vol. I, p. 157) and, together with Stephens, described the anatomy of the proboscis of *Glossina palpalis* (*Memoir* XVIII, p. 53), and subsequently (*Annals*, Vol. I, p. 169) that of *Stomoxys calcitrans*.

In 1906, a former student, Capt. R. Markham Carter, I.M.S., forwarded to Newstead a species of tsetse-fly (namely, *G. tachinoides*) from Arabia, this being the first observation of the occurrence of *Glossina* outside Africa.

In 1910, Newstead described three new species of *Glossina* (*Annals*, Vol. IV, p. 369), namely, *G. submorsitans*, *G. brevipalpis* and *G. fuscipes*. These new species were founded on an examination of the morphological characters of the male genital armature. A revision of *Glossina*, based on a study of this structure, was made (*Bull. Ent. Res.*, Vol. II, p. 9), and later two further new

species of this genus were described, namely, *G. austeni* (*Annals*, Vol. VI, p. 129, and *Bull. Ent. Res.*, Vol. III, p. 355) and *G. severini* (*Annals*, Vol. VII, p. 331).

In 1911, as a member of the Commission of the Royal Society to enquire into the relation of the African fauna to human trypanosomiasis, Newstead proceeded to Nyasaland, and for five months devoted himself to a study of the bionomics of the tsetse-fly (*Glossina morsitans*, West.), with a view to discovering its breeding grounds and devising means of checking its spread. The results of this investigation were published, jointly with Dr. J. B. Davey, in the Reports of the Commission, No. XV, p. 142. The physical features of the country were first described and an account given of the vegetation of the river and its borders, and the forest or fly area. The vertebrate fauna of the district were then dealt with. It was concluded that mpala antelopes supplied a very large proportion of the food necessary for the life and propagation of *Glossina*. Two species of birds were shown to prey upon *G. morsitans*. The breeding grounds of *G. morsitans* were thinly scattered over the whole of the country, and large numbers did not occur in any given spot. It was found by experiment that the average time between each meal was about two and a half days. The period that elapsed between the date of capture of the fly and the production of the larvae varied from two to twenty-nine days. The duration of the pupal period was found to be about twenty-five days. The period of chief activity of *G. morsitans* was between the hours of 10 a.m. and 4 p.m.

In 1919, Miss A. M. Evans made a study of the genital armature of the female *Glossina* (*Annals*, Vol. XIII, p. 31). In 1918, Newstead discovered that the innumerable papillae which form the sculpturing on the exterior of the prominent lobes at the anal extremity of the larvae of *Glossina* are respiratory openings, and evidently function as such during the inter-uterine life of the larva. Similar structures were found in the *Hippoboscidae* (*Annals*, Vol. IV, p. 93).

Jointly with Carter, a new genus and three new species of anopheline mosquitoes were described (*Annals*, Vol. IV, p. 377), namely, *Dactylomyia*, nov. gen., and *Dactylomyia ceylonica*, *Pyretophorus cardamatisi* and *Cellia cincta*, and later

six further new species and varieties were dealt with (*Annals*, Vol. V, p. 233). In 1911, Newstead and Carter founded a new genus of Culicinae from the Amazon region, which they named *Thomasina*. The type species, *Thomasina longipalpis*, had previously been referred by Newstead and Thomas to the genus *Mansonia*, but it was now found that the morphological characters of the palpi and tarsi were so markedly different from those of *Mansonia* that the species could no longer remain in that genus (*Annals*, Vol. IV, p. 553). Some mosquitoes of the genera *Banksinella* and *Taeniorhynchus* were described by Carter (*Annals*, Vol. VII, p. 581) with a view to establishing the affinities of certain species and in reference also to the synonymy adopted by other students of this group of blood-sucking insects. In 1920, Carter gave an account of the male genital armature of the British anopheline mosquitoes (*Annals*, Vol. XIII, p. 453). Extensive observations were made by Blacklock and Carter on the bionomics of *A. plumbeus* (*Annals*, Vol. XIII, p. 421). It was found to be essentially a tree-hole breeder; larvae were taken from the water in rot-holes of elm, sycamore and other trees, from 2 to 20 feet above the ground. The breeding-places may occur in more or less isolated trees situated sometimes within a few yards of houses. *A. plumbeus* feeds on man both day and night. The observers obtained larvae from tree-holes in December to February, and they ascertained that thirty-five out of forty larvae survived freezing for five to thirty minutes. (For infection experiments with *A. plumbeus*, see p. 12).

In 1912, Carter described three new species of the genus *Tabanus*, which he named *Tabanus nagamiensis*, *T. fulvicapillus* and *T. donaldsoni*, and in a subsequent study (*Annals*, Vol. IX, p. 173) eight previously undescribed Tabanidae were dealt with. He also described three new African midges (*Annals*, Vol. X, p. 131), *Forcipomyia lefanui*, *Culicoides cordiformitarsis* and *Culicoides stephensi*, and later (*Annals*, Vol. XII, p. 289) two others, *Culicoides ocrothorax* and *Forcipomyia ingrami*, a species of interest owing to the fact that, given favourable opportunities for attack, its larvae prey upon the larvae of mosquitoes breeding in rot-holes in trees. In 1920, Carter, Ingram and Macfie commenced an exhaustive study of the Ceratopogonine midges of the Gold Coast, with descriptions of new species. In the first account of

these midges (*Annals*, Vol. XIV, p. 187), after a description of the technique employed, the observers dealt with the bionomics of the various genera. The second instalment (*ibid.*, p. 211), which began a systematic account of the Ceratopogoninae, dealt with the genus *Culicoides*, and included descriptions of sixteen species, eleven of which were new. The larvae and pupae of several species were described in detail. The third account of this investigation (*ibid.*, p. 309) dealt with six new species belonging to three genera, of which one of the latter is new.

In 1919, an article on the blood-sucking *Nematocera* was contributed by Carter to 'The Practice of Medicine in the Tropics' (now in the press). This dealt with the biting flies of the families *Culicidae*, *Psychodidae*, *Chironomidae* and *Simuliidae*. The account included general considerations regarding structure and bionomics, the species of malaria-carrying *Anopheles* being arranged in groups according to the nature of the evidence on which they were incriminated, and the classification. In the last section, the diagnostic characters of all the known (one hundred and twenty) Anopheline mosquitoes were given in synoptic tables.

Newstead continued his researches on *Coccidae*, of which the British species formed the subject of a monograph, in two volumes, issued by him among the Ray Society publications, in 1900 and 1902. In 1908, he contributed an article on these insects to the reports of the Swedish Zoological Expedition to Kilimandjaro (Vol. II, Part 12); the same year he wrote of the scale insects and mealy bugs of Egypt (*Liv. Univ. Inst. Comm. Res. in the Tropics Quart. Journ.*, Vol. III, p. 14), and reported upon a collection of Coccidae affecting plants in Java and West Africa (*Journ. Econ. Biol.*, Vol. III, p. 32). In 1910 and 1911, he described two new species of African coccids (*Journ. Econ. Biol.*, Vol. V, p. 18), reported on a collection from Uganda (*Bull. Ent. Res.*, Vol. 1, pp. 63 and 185), on another from South and South-west Africa, and on a third in the Berlin Zoological Museum (*Mitt. aus dem Zool. Mus. in Berl.*, Vol. V, p. 155). Later, he commenced a series of studies on Coccidae, which are still being pursued (*Bull. Ent. Res.*, 1913-1920). In these papers, over one hundred and sixty different species were dealt with, including the descriptions, with illustrations, of one hundred and six species and varieties new to science; the major portion of these are serious pests to various crops under

cultivation in tropical and sub-tropical countries. In 1910, Newstead served on the Special Commission appointed by the Government of Malta to suggest means for stamping out the fluted scale insect (*Icerya purchasi*), then threatening the orange-growing industry of the island. Regulations for the suppression of the pest were drafted and circulated.

Other work of an economic nature undertaken by Newstead included an investigation into the food of some British birds (*Suppl. to Journ. of Board of Agric.*, Vol. XV). This work, which had extended over a period of twenty years, was based upon over eleven hundred records, chiefly *post mortem*. His tentative verdict was in favour of the birds, the records showing what an important part is played by the majority of British birds in checking the increase and lessening the ravages of many insect pests of plants and crops. In 1910, Newstead dealt with some insects affecting cultivated plants in the West Indies (*Journ. Roy. Hort. Soc.*, Vol. XXXVI, p. 53), and in 1913, jointly with Bruce Cummings, issued a paper on a gall-producing Psyllid from Syria (*Ann. Mag. Nat. Hist.*, Vol. XI, p. 306).

In 1910, Newstead went to Malta to investigate sand flies of the genus *Phlebotomus*, the main object being to discover the chief breeding-places of these insects, and to recommend practical measures for destroying them in the larval stage. It was discovered that four distinct species of *Phlebotomus* occur in the island, previous investigators having notified one species only. The discovery of some important structural details concerning the anatomy of these insects was made and a long series of drawings illustrative of the salient characteristics was prepared, as well as a series illustrative of the internal anatomy (*Annals*, Vol. V, p. 139). Later, he described some new species (*Bull. Ent. Res.*, Vol. III, p. 361, Vol. V, p. 179, Vol. VII, p. 191, and Vol. XI, p. 305), and in 1913 dealt with three West African species (*Bull. Soc. Path. Exot.*, Vol. VI, p. 124).

Besides the special studies noted above, many articles on entomological subjects were contributed to a variety of journals by the Department of Entomology. In addition, innumerable collections of insects submitted by the Imperial Bureau of Entomology, by the Belgian Government, and from other sources, were examined and identified.

In 1915, Newstead went to France and Flanders, there to

organise measures of fly control. A report of this work was submitted to the War Office.

By the request of the Royal Society, Newstead and others commenced in 1916 an investigation into the problems connected with the damage caused to grain and flour during transit and in storage. It was found that wheat and flour are liable to attacks and injury by acarids, of which *Aleurobius farinae* was most commonly encountered. It was established that mites will not injure wheat and flour in which the moisture content is 11 per cent. or under, whatever the temperature may be. The morphology and bionomics of the infesting mites were studied, and experiments carried out with regard to methods of destruction. Newstead and Morris also reported upon the non-parasitic or forage acari of the family *Tyroglyphidae*, to which Pillers added clinical notes derived from veterinary experience (*Royal Society*: *Reports of the Grain Pests* (*War*) *Committee*, Nos. 2 and 8).

David Thomson made feeding experiments with the European bed bug (*Cimex lectularius*) in various diseases (*Annals*, Vol. VIII, p. 19). He found that protozoa were absent from the gut of this species (one hundred and eighty-four examined). No acid-fast bacilli were found in one hundred and five bed bugs fed on lepers, nor in thirty-five others caught in bed mattresses of leper patients. Nothing abnormal was found in bugs fed on cases of lymphadenoma, carcinoma and malaria. Forty bugs fed on a case of spleno-medullary leukaemia all developed numerous Charcot-Leyden crystals in their intestines.

Dutton, Todd and Christy described the Congo floor maggot, a blood-sucking dipterous larva found in the Congo Free State (*Memoir* XIII, p. 49). The larva was stated to be semi-translucent, of a dirty white colour, acephalous, amphipneustic, consisting of eleven segments, and to feed mainly, or entirely, at night. The duration of the pupal stage was a fortnight to three weeks. A light-brown fly, caught in many huts infested with the maggot, was subsequently identified by Austen as *Auchmeromyia luteola*. Newstead (*Annals*, Vol. I, p. 49) noted that the true larval stage is continued till after the formation of the puparium, and that a large percentage of the flies escape backwards from it.

In addition to dealing with the anatomy and bionomics of

Ornithodoros moubata, the tick transmitting African relapsing fever (already mentioned above), Newstead, jointly with Todd, described a species of acarid found infecting the lungs of monkeys, namely, *Pneumonyssus duttoni* (*Memoir* XVIII, p. 41), and later he described another new acarid, *Pneumonyssus griffithi*, found in the lungs of the Rhesus monkey (*ibid.*, p. 47).

PROTOZOOLOGY

Dutton, Todd and Tobey gave an account of certain parasitic protozoa observed by them in Africa (*Memoir* XXI, p. 87, and *Annals*, Vol. I, p. 285) in mammals, birds and reptiles, including full descriptions and figures of some forms of *Leucocytozoon ziemanni*, parasitic in a grey hawk of the Congo. Fantham studied the leucocytozoon, *L. lovati*, of the red grouse, *Lagopus scoticus*, and observed the occurrence of schizogony in its life cycle (*Annals*, Vol. IV, p. 255). He also studied a flagellate found in the alimentary tract of the body louse, which he named *Herpetomonas pediculi* (*Annals*, Vol. VI, p. 25), and of which he demonstrated the complete life cycle, notifying its occurrence in lice in England, as well as in India and Tunisia (*ibid.*, p. 403). Another Herpetomonas, *H. stratiomyia*, sp. n., was discovered by Fantham and Porter (*Annals*, Vol. VII, p. 609) parasitic on the larvae, pupae and imagines of the flies *Stratiomyia chameleon* and *S. potamida*. Research into induced herpetomoniasis in birds resulted in producing this condition in canaries, sparrows and martins by feeding them on insects containing herpetomonads; in some cases the infection was fatal. It was found that the cycle of the flagellate in the avian host resembled morphologically that in the insect (*Annals*, Vol. IX, p. 543). Fantham and Porter studied the effects on their hosts of certain *Myxosporidia* inhabiting the gall bladders of various fish (*Annals*, Vol. VI, p. 467). In 1916, Fantham contributed the section on the Protozoa to 'The Animal Parasites of Man,' issued jointly with Stephens and Theobald.

Seidelin described some blood parasites in reptiles (*Annals*, Vol. V, p. 371), and also some species of *Klossiella* in the kidney of a guinea-pig (*Annals*, Vol. VIII, p. 553). E. H. Ross observed the development of a leucocytozoon in a guinea-pig, for which he

proposed the name *Lymphocytozoon cobayae* (*Proc. Roy. Soc.*, B., Vol. LXXX, p. 67); Sinton prosecuted research into the morphology and biology of *Prowazekia urinaria* (*Annals*, Vol. VI, p. 245); and O'Farrell, in a study of hereditary infection, with special reference to its occurrence in *Hyalomma aegyptium* infected with *Crithidia hyalommae*, gave an account of the four periods in the life cycle of this flagellate (*Annals*, Vol. VII, p. 545).

In 1917, Smith and Matthews investigated the incidence of intestinal protozoa in two hundred and fifty patients admitted to hospital for diseases other than dysentery (*Annals*, Vol. X, p. 361). *Entamoeba histolytica* was found in 8 per cent. of the cases, *E. coli* in 19·2 per cent., *G. intestinalis* in 8 per cent., *C. mesnili* in 2 per cent., and *T. intestinalis* in 1·7 per cent. Of the two hundred and fifty cases examined, two hundred and two were suffering from non-intestinal complaints, and of this number 9·4 per cent. were found to be harbouring cysts of *E. histolytica*. Among ninety-one men who had been to France only, two were discovered to be 'carriers' of *E. histolytica*. In a further investigation (*Annals*, Vol. XI, p. 183), two hundred non-dysenteric patients were examined, and protozoal infections found in 34·5 per cent.; *E. histolytica* in 7·5 per cent. Matthews described and figured the characteristic morphological features of cysts of the common intestinal protozoa of man (*Annals*, Vol. XII, p. 17), and later made a mensurative study of the cysts of *E. coli* (*Annals*, Vol. XII, p. 259), and traced the course and duration of an infection with this parasite (*Annals*, Vol. XIII, p. 17). Matthews and Smith investigated the spread and incidence of intestinal protozoal infections in the population of Great Britain. The first selected population consisted of four hundred and fifty civilians in the Liverpool Royal Infirmary (*Annals*, Vol. XII, p. 349), of which 1·5 per cent. were found to harbour *E. histolytica* and 6·7 per cent. *E. coli*. The figures for army recruits, of which one thousand and ninety-eight cases were examined, were *E. histolytica* 5·6 per cent., *E. coli* 18·2 per cent., *E. nana* 2·4 per cent., *G. intestinalis* 6·0 per cent., and *C. mesnili* two cases. In five hundred and forty-eight children, all under the age of twelve (*Annals*, Vol. XII, p. 361), *G. intestinalis* was the parasite most commonly found. Of two hundred and seven male asylum patients (*Annals*, Vol. XIII,

p. 91), 9·7 per cent. were found to be infected with *E. histolytica*, 45·9 per cent. with *E. coli*, and 23·2 per cent. with *C. mesnili*. University and School cadets were also examined; the same protozoa were found as amongst other series, but the number of cases recorded was too small to allow of conclusions being drawn as to incidence amongst this higher social class.

In 1906, Drs. Fantham and Porter investigated the Isle of Wight bee disease (*Annals*, Vol. VI, p. 163). It was found that the disease was due to a minute microsporidian parasite, *Nosema apis*, sp. n., which gained access by the mouth to the intestines. Experimental work proving the pathogenicity of the parasite was carried out. It was found that *Nosema apis* was harboured by other insects besides the hive bees (*Annals*, Vol. VII, p. 569). It was considered that a bee, itself apparently immune, can be a parasite carrier. A morphological study of *Nosema apis* was made, and the two phases in its life cycle demonstrated: (1) a multiplicative phase, termed merogony, which occurs in the epithelium of the chyle stomach and intestines of the bee; (2) a second phase, termed sporogony, leading to the formation of minute, resistant resting spores, which are shed in the faeces of the bee, fouling the surroundings of the hive and producing infection of fresh bees when swallowed in food or drink. An allied organism, *Nosema bombi*, sp. n., parasitic in, and pathogenic to, bumble bees, was discovered, and its life cycle, and suggested economic measures of control, set forth in a subsequent paper (*Annals*, Vol. VIII, p. 623).